

CLAIMS

1/ Compound capable of cross-linking a stimulatory receptor with a KIR.

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2/ Compound according to claim 1, characterized in that it is capable of specifically regulating the activation of a KIR.

10 3/ Compound according to claim 1 or 2, characterized in that it is capable of regulating the activation of a stimulatory receptor.

15 4/ Compound according to any of the preceeding claims characterized in that said stimulatory receptor is an ITAM-bearing receptor such as KAR, FcεRI, CD3/TCR, CD16, receptors related to tyrosine kinase activities or a receptor sub-unit such as CD3ζ, CD3ε, CD3γ, CD3δ or FcεRIγ.

20 5/ Compound according to any one of claims 1-4, characterized in that said KIR is a IgSF member, particularly selected from the group comprising CD158, CDw159, CDw160, or said KIR is lectin-like, such as the CD94-NKG2A/ B heterodimer.

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6/ Compound according to any of the preceeding claims, characterized in that said KIR is expressed on a NK cell, on a T cell, on a mast cell or on a monocyte or is recombinantly expressed.

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7/ Compound according to any of the preceeding claims, characterized in that it is capable of inducing the regulation of free calcium concentration in a cell, particularly of inducing the regulation of calcium influx
35 into a cell and/or of inducing the regulation of calcium mobilization from intracellular compartments.

8/ Compound according to any of the preceeding claims, characterized in that it is capable of inducing the recruitment by said KIR or KIR homologue of a phosphatase selected from the group consisting of SHP-1, SHP-2.

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9/ Compound according to any of the preceeding claims, characterized in that it is essentially a polypeptide, a glycoprotein or a carbohydrate.

10/ Compound according to any of the preceeding claims, characterized in that said compound is a bispecific reagent and/or a chemical inducer of dimerization.

11/ Compound according to any of the preceeding claims, characterized in that said compound is a bispecific antibody, comprising at least one Fab, Fd, Fv, dAb, CDR, F(ab')₂, VH, VL, ScFv fragment.

12/ Compound according to any of the preceeding claims, characterized in that it is capable of cross-linking said KIR with said stimulatory receptor in the extracellular domain of a cell.

13/ Compound according to any of the preceeding claims, characterized in that it is capable of crossing through a lipid bi-layer, and is liposoluble and/or associated with a drug-delivery system.

14/ Compound according to any of the preceeding claims, characterized in that it is capable of cross-linking said KIR with said stimulatory receptor in the intracellular domain of a cell.

15/ Compound according to any of the preceeding claims, characterized in that it is capable of modulating the

release of serotonin and/or of inflammatory mediators by a cell expressing FcεRI, such as a mast cell, and/ or of modulating cytokine release, such as Interleukin-6, Tumor Necrosis Factor Alpha release, from a cell such as a mast
5 cell or a NK cell and/or of modulating interleukin production such as the IL-2 production and/or the γ-interferon production from a peripheral blood cell and/or of modulating the proliferation of peripheral blood cells.

10 16/ Compound according to any of the preceeding claims, characterized in that it is capable of controlling the host tolerance to allogeneic grafts and/or the graft toxicity against a host tissue.

15 17/ Nucleic acid coding for a polypeptide according to any one of claims 9-16.

18/ Cell transfected by a nucleic acid according to claim 17.

20 19/ Pharmaceutical preparation comprising a compound according to any one of claims 1-16 or a nucleic acid according to claim 17 or a cell according to claim 18 in a physiologically acceptable vehicle, in a therapeutically-
25 effective amount useful for modulating an animal cell function involved in a disease selected from the group consisting of immunoproliferative diseases, immunodeficiency diseases, cancers, autoimmune diseases, infectious diseases, viral diseases, inflammatory
30 responses, allergic responses or involved in organ transplant tolerance.

20/ Method for the *in vitro* or *ex vivo* diagnosis of a cell
disregulation, comprising the step of estimating of the
35 relative proportion of co-aggregated KIR vs. non-co-aggregated KIR by:

- contacting a biological sample with a compound according to any one of claims 1-16 or with a nucleic acid according to claim 17 or a cell according to claim 18, and
- revealing the reaction product possibly formed.